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<p>(21) International Application Number: PCT/FI89/00105</p> <p>(22) International Filing Date: 12 June 1989 (12.06.89)</p> <p>(30) Priority data: 883197 5 July 1988 (05.07.88) FI</p> <p>(71) Applicant (for all designated States except US): BIOCON OY [FI/FI]; Runeberginkatu 3 A, SF-33710 Tampere (FI).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): TÖRMÄLÄ, Pertti [FI/FI]; Runeberginkatu 3 A, SF-33710 Tampere (FI). VAINIONPÄÄ, Seppo [FI/FI]; Orapihlajatie 21-27 B 12, SF-00320 Helsinki (FI).</p> <p>(74) Agent: KAHILAINEN, Hannu; Tampereen Patenttitoimisto Oy, Kanslerinkatu 6, SF-33720 Tampere (FI).</p>		<p>(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), FI, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published With international search report.</p>
<p>(54) Title: REINFORCED POLYMERIC BIOMATERIAL FILMS</p> <div data-bbox="427 1081 1153 1554"> <p>A fibril (a bundle of microfibrils)</p> <p>crystalline blocks</p> <p>group of lamellae</p> <p>Transformation of lamellar structure to fibrillar structure</p> </div> <p>(57) Abstract</p> <p>This invention describes absorbable and/soluble nonporous or porous polymeric films which have been reinforced with at least partially absorbable and/or soluble oriented structural elements like with oriented molecular chains, crystalline lamellae or filaments or fibers or with structures which have been constructed of fibers. The films of this invention are applied either to join tissues or their parts to each others or to separate them from each others like specially to protect controlled growth of periodontal ligament and/or cementum tissue.</p>		

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Reinforced Polymeric Biomaterial Films.

The invention relates to an absorbable and/or soluble
5 polymeric film.

Polymeric biomaterials like films (or membranes) have
several application possibilities in surgical
treatment. Porous or nonporous polymer film can be
10 applied e.g. to support from outside an operated or
damaged tissue or organ or their part e.g. by fixing
the supporting film by tissue adhesive or by suturing
around the operated internal organ. Porous or nonporous
film can be applied also to separate inflamed tissues
15 or organs or their parts from their environment and
in this way to prevent the spreading of infection.
Separating films can be applied also to separate cell
tissues from each others and at the same time to
guide in a controlled way the growth of the cells.
20 Such a typical application is the use of polymer film
to separate infected, surgically cleaned root of the
tooth from the gingival connective tissue and
epithelium. Then the periodontal ligamentum -and
cementum tissue can grow into the coronal direction
25 on the surface of the healing root, which leads to a
new fixation of the tooth. In this way the periodontal
structures can be regenerated (J. Gottlow, S. Nyman,
J. Lindhe, T. Karring and J. Wennström, J. Clin.
Periodontol., 13 (1986) 204). After a periodontal
30 surgical operation there are four types cell tissues
which try to cover the surface of the root of the
tooth. In an uncontrolled situation the epithelium
grows first along the surface of the root and prevents
the refixation of the tooth. Also the connective
35 tissue of the gingiva can fix on the surface of the
root. However, without the cementum or periodontal
ligament the fixation is weak and can lead to the
breaking of the fixation (S. Nyman, T. Karring, J.
Lindhe and S. Planten, J. Clin. Periodontol., 7 (1980)

394; T. Karring, F. Isidor, S. Nyman and J. Lindhe, J. Clin. Periodontol., 12 (1985) 51).

5 The cells which produce cementum and periodontal
ligament grow so slowly that they usually don't grow
on the surface of the infected root of the tooth
before gingival tissue and epithelium. However, the
studies of guided tissue regeneration have shown that
cells, which produce cementum, can grow on the surface
10 of the root, if the surface of the root has been
isolated of other tissues during the healing (S.
Nyman, J. Gottlow, T. Karring and J. Lindhe, J. Clin.
Periodontol., 9 (1982) 275).

15 In surgical use are known biostable films, which act
as a protecting layer between the gingival connective
tissue and the root of the tooth. Such films form a
protected space on the defect of the root. In this
space the remaining cells of periodontal ligament can
20 cover selectively the surface of the root. E.g. Gore-
Tex is such a biostable film material. It is
polytetrafluoroethylene (PTFE) film, which comprises
PTFE nodules and fine fibrils which connect the nodules
to each others. Such biostable films or membranes
25 must, however, be removed with an other operation
after the healing of the root of the tooth. The
removal operation must be carried out typically 1-3
months after the first operation. This means
significant economical costs and additional risks
30 (e.g. infections) to the patient.

An ideal film or membrane to protect the growth of
the cells which produce cementum and periodontal
ligament on the root of the tooth, is an absorbable
35 and/or soluble (biodegradable) film or membrane,
which is digested by the metabolism of the living

cells and/or by the solution without causing tissue reactions which should prevent the healing. In this case the need of the second operation is eliminated.

5 Among biomaterials experts it is known to use melt-molded or solution evaporated absorbable films to separate tissues, organs or their parts from each others or to support operated or damaged tissues or organs or their parts from their outer surface.

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Accordingly it is known to use polylactide film which has been manufactured of chloroform solutions of polylactide by evaporation, to separate the healing surface of the root of the tooth from the gingival connective tissue and the epithelium. In such a situation the periodontal ligamentum- and cementum tissue can grow into the coronal direction under the protection of the polylactide film, which leads to a new connective tissue fixation (I. Magnusson, C. Batich and B.R. Collins, J. Periodontol., January, 1988, p. 1). Such polymer films are, however, weak of their mechanical strength (tensile strength typically 40-60 MPa). This leads to practical difficulties in the surgical use of such films. Such difficulties are e.g.

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- Mechanically weak films break or tear easily when they are installed into the living tissue in a surgical operation. On the other hand, if the surgeon wants to secure that such a film doesn't break or tear during the operation, thick films (the thickness typically 50-500 μ m) must be used. Such films are stiff and therefore it is difficult to put the film tightly on the surface of the root. On the other hand, such films form a considerable amount of foreign material in the

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tissues, which may lead to a foreign body reaction, which may delay, disturb or prevent healing at least partially.

- 5 - The fixation of mechanically weak film on the surface of the root of the tooth by e.g. sutures which penetrate the film is difficult, because the suture can cut the weak film easily when it is drawn through the hole in the film. This may lead
10 to tearing of the film and to the loosening of the suture during the operation.

The main reason to the poor mechanical strength properties of absorbable polymeric films which are
15 manufactured by melt-molding or solution evaporation is that when the melt solidifies or the solution evaporates the crystallizing polymer transforms to a partially crystalline, spherulitic structure. Accordingly the partially crystalline, absorbable
20 film, which has been manufactured by melt-molding or by evaporating, comprises typically folded molecular chain lamellae (the thickness 100-300 Å, the breadth about 1 µm), which are surrounded by amorphous polymer. The lamellae, on the other hand, are formed
25 of mosaic-like folded chain blocks (the breadth a few hundred Å). The lamellae join typically to ribbon-like structures, which grow from the crystallization nuclei into three-dimensional sphere-like spherulitic structures. Because polymeric materials with
30 spherulitic structure usually do not show significant orientation of polymeric chains in some special direction, the strength properties of such polymer materials are typically quite modest (e.g. tensile strength typically 20-60 MPa).

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In this invention it has been found unexpectedly, as stated in the characteristic part of the independent claim, that when an absorbable and/or soluble film

(or membrane) is reinforced with at least partially absorbable and/or soluble oriented structural elements, one can create new strong and tough absorbable and/or soluble films, which have at least partially oriented structure, and which can be used better than the known materials to support or to join tissues or organs or their parts and/or to separate them from each others. Such films can be used e.g. as a separating film on the surface of the root of the tooth to protect the controlled growth of periodontal ligamentum- and/or cementum tissue.

The oriented structural elements mean in this connection the at least partially oriented polymeric molecule chains or their parts, oriented crystalline lamellae, spherulites or their parts, fibrils etc. morphological structure-elements or their parts and fibers, filaments, film-fibers, threads, braids, non-woven structures, networks and meshes, knits or woven structures or corresponding fiber constructions.

Further this invention describes a method, as stated in the characteristic part of the independent claim related to the method, to manufacture at least partially oriented, absorbable films by orientation at least part of the structural reinforcement elements of the material into the desired direction by means of the flow of the material and/or by mechanical deformation or by reinforcing the continuous or noncontinuous matrix by means of absorbable and/or soluble fibers, film-fibers or by means of structures which are constructed of them. Materials such as filaments, fibrils, threads, non-woven structures, meshes and networks, knits or woven structures can be used.

Further in this invention has been described the use the films of the invention as surgical implants to

separate tissues and/or organs and/or their parts from each others or to support them. The use can be related to protect the controlled growth of the periodontal ligament and/or cementum tissues.

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The invention will now be described in detail in the following description. References are made to the enclosed drawings, in which

10 Fig. 1a shows the transformation of a group of lamellae to a fibrillar structure,

Fig. 1b shows the molecular structure inside the microfibrils and between the same,

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Fig. 1c shows schematically the structure of a fibrillated polymer,

20 Fig. 2 shows schematically structural units found in a fibrillated structure,

Fig. 3 shows a sectional view of one embodiment of the film in accordance with the invention and

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Fig. 4 shows schematically the testing method used in connection with the examples.

30 The orientation and fibrillation of spherulitic polymer systems is a process, which has been studied extensively in connection with the manufacturing of thermoplastic fibers. E.g. The invention U.S. Pat. 3 161 709 describes a three phases drawing process, where the melt molded polypropylene filament is
35 transformed to a fiber with high mechanical strength.

The mechanism of the fibrillation is of its main features the following one (C.L. Choy et al. Polym.

Eng. Sci., 23 1983, p. 910). When a semicrystalline polymer is drawn, the molecular chains in the crystalline lamellae are aligned rapidly along the draw direction. At the same time, the spherulites are elongated and finally broken up. Crystalline blocks are torn off from the lamellae and are connected by taut tie-molecules originating from partial unfolding of chains. The alternating amorphous and crystalline regions, together with the taut tie-molecules, therefore form long thin (ca. 100 Å width) microfibrils which are aligned in the draw direction. Since the intrafibrillar tie-molecules are created at the interfaces between crystalline blocks, they lie mainly on the outside boundary of microfibrils. Tie-molecules which linked different lamellae in the starting isotropic material are now connecting different microfibrils, i.e., they become interfibrillar tie-molecules locating at the boundary layers between adjacent microfibrils. Figure 1a shows schematically, how a group of lamellae is transformed to a fibrillar structure (to a fibril which comprises a group of microfibrils) as a consequence of drawing and Figure 1b shows schematically the molecular structure inside of microfibrils and between them. Figure 1c shows schematically the structure of fibrillated polymer. This Figure shows several fibrils (one of them has been coloured grey because of clarity) which comprise several microfibrils with the length of several micrometres.

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The fibrillar structure is already at relatively low draw ratios λ (where λ = the length of the sample after drawing/the length of the sample before drawing). E.g. HD-polyethylene is clearly fibrillated with the λ value of 8 and polyacetal (POM) with the λ value of 3.

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When the drawing of the fibrillated structure is further continued (this stage of the process is called often ultra-orientation), the fibrillar structure is deformed by shear displacement of microfibrils, giving
5 rise to an increase in the volume fraction of extended interfibrillar tie-molecules. If the drawing is performed at high temperature, the perfectly aligned tie-molecules will be crystallized to form axial crystalline bridges connecting the crystalline blocks.

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The excellent strength and elastic modulus values of the fibrillated structure are based on the strong orientation of polymer molecules and molecular segments into the direction of the drawing (into the direction
15 of the long axis of microfibrils).

Figure 2 shows schematically following structural units which can be seen in the fibrillated structure of polymer fibers and also in the structure of
20 macroscopical, fibrillated polymer samples like rods and tubes: crystalline blocks which are separated from each other by amorphous material (e.g. free polymer chains, chain ends and molecular folds), tie-molecules, which connect crystalline blocks with each other (the
25 amount and thickness of tie-molecules increases with increasing draw ratio λ) and possible crystalline bridges between crystalline blocks. Bridges can be formed during drawing when tie-molecules are oriented and grouped themselves to bridges (C.L. Choy et al.
30 J. Polym. Sci., Polym. Phys. Ed., 19, 1981, p. 335-352). Because the oriented structure contains in the orientation direction a big amount of strong covalent bonds between the atoms of the polymer chains, such material has in the orientation direction significantly
35 higher strength values than the nonoriented material has.

The oriented fibrillated structure which is shown in Figures 1 and 2 develops already at so-called natural draw ratios $\lambda < 8$. When the drawing is continued after this as an ultraorientation at a high
5 temperature, the amount of crystalline bridges can increase very high and in the extreme case bridges and crystalline blocks form a continuous crystalline structure. The effects of tie-molecules and bridges are often similar and therefore their exact
10 discrimination from each other is not always possible.

Orientation and fibrillation can be characterized experimentally by means of several methods. The orientation function f_c , which can be measured by
15 means of x-ray diffraction measurements, characterizes the orientation of molecular chains of the crystalline phase. f_c Attains as a rule already at natural drawing ratios ($\lambda < 6$) the maximum value 1. The polymeric material with spherulitic structure shows $f_c \ll 1$.

20 Birefringence (Δ) which can be measured by means of polarization microscope is also a quantity, which describes molecular orientation of molecular chains. As a rule it grows strongly at natural draw ratios
25 ($\lambda < 6$) and thereafter during ultraorientation more slowly, which shows that the molecular chains of the crystalline phase are oriented into the drawing direction at natural draw ratios and the orientation of molecules in the amorphous phase continues further
30 at higher draw ratios (C.L. Choy et al. Polym. Eng. Sci., 23, 1983, p. 910-922).

For unidirectionally oriented films is typical that the strength properties of the film are perpendicular
35 to the orientation direction significantly weaker than in the orientation direction. Therefore according to an advantageous embodiment of this invention the orientation of the film is made biaxially in the

direction of the plane of the film either (a) by rolling and/or drawing the thick film thinner between rollers or (b) by drawing the film simultaneously into different directions (usually in directions which are perpendicular to each others). Two-dimensional orientation creates oriented, reinforcing structural elements in the plane of the film in different directions, which makes also the strength properties of the film in perpendicular direction better.

Also other orientation methods can be applied to manufacture the films of this invention. Polymeric melt can be e.g. crystallized in a rapidly flowing state, so that the flow orientation is frozen at least partially into the solid film to reinforce it.

In addition to the above methods, where the reinforcing structural elements are created into polymer matrix during its deformation, it is also possible to apply earlier manufactured reinforcing elements to reinforce the films of the invention. Such typical structural elements are absorbable and/or soluble fibers, filaments, fibrils, film-fibers, threads, cords, non-woven structures, webs and meshes, knits, woven structures or corresponding. In these cases the absorbable and/or soluble film can be manufactured by several different methods. E.g. the reinforcing fibers or corresponding and the film forming matrix polymer can be compressed together by means of heat and pressure, which gives a film which is reinforced with fibers or with corresponding structures. It is also possible to immerse the fibers with a solution of a polymer and to evaporate the solvent at least partially and to press the fibers by means of pressure and possibly also with heat into a fiber reinforced film. It is also possible to melt the fiber construction at least partially and to compress the material into at

least partially self-reinforced film. For all the previous films it is typical that because of strong, oriented structural elements these films have significantly better toughness and strength properties than the non-oriented films have.

The orientation of amorphous absorbable and/or soluble polymers does not lead to as strong increase of strength than the orientation of partially crystalline films. However, also the mechanical deformation of amorphous films leads to the increase of their strength in the direction of the deformation, because the molecular chains are also oriented in this case. However, a specially strong reinforcing effect is obtained to amorphous absorbable films only when they are reinforced with absorbable fibers or with corresponding structures as the examples of this invention show.

Table 1 shows some absorbable and/or soluble polymers, which can be applied as raw materials (both as oriented structural elements and as film matrix) in manufacturing of the films of this invention.

The films can be nonporous or they may have pores, which can be created (a) with methods known in polymer technology, like e.g. by means of different additives like gases or easily evaporating solvents etc., (b) by constructing the film mainly of fibrous structural units or (c) by perforating the film (by making holes into the film).

Table 1. Absorbable and/or soluble polymers

	Polymer
5	Polyglycolide (PGA)
	<u>Copolymers of glycolide:</u>
	Glycolide/L-lactide copolymers (PGA/PLLA)
10	Glycolide/trimethylene carbonate copolymers (PGA/TMC)
	Poly lactides (PLA)
15	<u>Stereocopolymers of PLA:</u>
	Poly-L-lactide (PLLA)
	Poly-DL-lactide (PDLLA)
	L-lactide/DL-lactide copolymers
20	<u>Copolymers of PLA:</u>
	Lactide/tetramethylglycolide copolymers
	Lactide/trimethylene carbonate copolymers
	Lactide/ δ -valerolactone copolymer
	Lactide/ ϵ -caprolactone copolymer
25	Polydepsipeptides
	PLA/polyethylene oxide copolymers
	Unsymmetrically 3,6-substituted poly-1,4-dioxane-2,5-diones
30	Poly- β -hydroxybutyrate (PHBA)
	PHBA/ δ -hydroxyvalerate copolymers (PHBA/HVA)
	Poly- β -hydroxypropionate (PHPA)
	Poly-p-dioxanone (PDS)
35	Poly- δ -valerolactone
	Poly- ϵ -caprolactone
	Methylmethacrylate-N-vinyl pyrrolidine copolymers
	Polyesteramides
	Polyesters of oxalic acid
40	Polydihydropyrans
	Polyalkyl-2-cyanoacrylates
	Polyurethanes (PU)
	Polyvinylalcohol (PVA)
	Polypeptides
45	Poly- β -malic acid (PMLA)
	Poly- β -alkanoic acids
	Polyvinylalcohol (PVA)
	Polyethyleneoxide (PEO)
50	Chitine polymers

Reference: S. Vainionpää, P. Rokkanen and P. Törmälä, Progr. Polym. Sci., in press.

It is self-evident that also other absorbable and/or soluble polymers than those given in Table 1 can be applied in manufacturing the films of this invention.

5

The films of this invention can contain or in structures which form part of them can be also combined different bioactive additives like antibiotics, growth hormones, drugs, hemostatic chemicals and/or other therapeutic components which have advantageous effects upon the healing of tissues.

It is possible also to combine and/or to connect to the films of this invention other materials like biostable fibers, fiber constructions, films etc. to achieve the desired effects in different surgical operations.

According to one advantageous embodiment the film of the invention is formed of nonporous outer surfaces and of a middle layer which contains at least partially closed porosity (Figure 3). Such a film is flexible and mechanically strong and internal porosity of the film can be at least partially filled with bioactive substances like antibiotics, drugs, growth hormones, hemostatic additives, chemotherapeutic substances etc. which can be released from the film into the surrounding tissues in a controlled way.

The invention is illustrated by means of the following nonlimiting examples.

EXAMPLE 1.

A single screw extruder (the screw diameter 25 mm) was applied to manufacture plane films of absorbable and soluble polymers and polymer mixtures by using the slot-die (the slot breadth 20 mm, the height 0.4

mm). The films were cooled with nitrogen gas blow and they were oriented biaxially either (a) by rolling them between heated rollers to the thicknesses 2 μm - 40 μm or (b) by drawing the films simultaneously in the manufacturing direction of film and in the perpendicular direction. The rolling temperatures and drawing temperatures were above the glass transition temperatures and below the melting temperatures of the materials and material mixtures. The deformation grades were between the drawing ratios 1.5 - 4. Oriented films were manufactured of absorbable and/or soluble materials given in Table 2. The tensile strengths of oriented and nonoriented corresponding films were compared to each others. From this basis was defined the relative tensile strength of the oriented films (R.T.S. = the tensile strength of the oriented film in the orientation direction/the tensile strength of the nonoriented film).

Table 2. The relative tensile strengths (R.T.S.) and the relative tear strengths (R.Tr.S.) of oriented films.

The oriented film	The thickness of the oriented film (μm)	R.T.S. R.Tr.S.	
PGA	4	6	3
PGA/PLLA	20	5.4	3
PGA/TMC	40	3	2
PLLA	20	6	4
PDLLA	60	2	1.5
PHBA	50	3	2
PHBA/HVA	50	2	1.6
PDS	60	3	2
PVA	40	2	1.5

The tearing effect of the multifilament suture (Dexon[®], size 0 (USP), manufacturer Davis & Geck, Gosport, England) upon the oriented and nonoriented films was studied by making into the film a small hole with a needle at the distance of 10 mm from the edge of the film, by drawing the suture through the hole, by knotting the suture into a loop and by tearing the suture loop through the film (see Figure 4).

10

The relative tear strength (R.Tr.S) of the oriented films was defined:

R.Tr.S=

Tear force of oriented film/Thickness of film
15 Tear force of nonoriented film/Thickness of film

Table 2 gives the studied materials, the thicknesses of the oriented films, their relative tensile strengths and relative tear strengths.

20

Table 2 shows that the tensile and tear strengths of the oriented films are superior in comparison to the corresponding properties of nonoriented films.

25 EXAMPLE 2.

The PGA, PGA/PLLA, PGA/TMC, PLLA and PDS polymers of Table 2 were used to manufacture with so-called blow-film technique oriented absorbable films by melting the materials with a single screw extruder, by pressing the melt with pressure through a ring-like die into a tube-like preform (diameter 60 mm, the thickness of the wall 0.4 mm) and by orienting the material biaxially by means of an internal overpressure during the solidifying of the material (the thicknesses of the oriented films were between 40 µm and 80 µm).

30
35

The relative tear strengths of the oriented films had values about three.

EXAMPLE 3.

5 Absorbable fibers or sutures which were braided of them (thicknesses 20 μm - 400 μm) were woven into plain weave type loose fabrics. The fabric was cut into pieces (20 mm x 80 mm) and these pieces were compressed
10 together with absorbable and/or soluble films which were manufactured of absorbable and/or soluble polymers by melting or by evaporating from solvent. During the compression the pressure (80 MPa) and heat (if necessary) was applied. The compression conditions
15 were selected in such a way that the film material softened and/or melted and wetted the fibers. The relative tensile strengths of the fiber reinforced films (thicknesses 30 - 2000 μm) were measured in comparison to the strength values of the non-reinforced
20 matrix polymer films (according to the Example 1). Table 3 shows the studied matrix polymers, reinforcement fibers and the relative tensile strengths (R.T.S.) of the oriented films.

25 The tear strengths of reinforced and non-reinforced films were studied according to the method of the Example 1. When the fiber reinforcement was made with PHBA and PHBA/HVA fibers the relative tear strengths of fiber-reinforced films were between 8 and 20. In
30 the case of absorbable films reinforced with PGA, PGA/TMC, PGA/PLLA, PLLA and PDS fibers, the tearing suture broke before the total breaking of the film.

The measurements of Example 3 showed the superior
35 tensile and tear strengths of the reinforced films in comparison to the non-reinforced films.

Table 3. The structural components and the relative tensile strengths (R.T.S.) of fiber reinforced absorbable and/or soluble films.

5	<u>Matrix polymer</u>	<u>Fiber reinforcement</u>	<u>R.T.S.</u>
	PDS	PGA	8
	PDS	PGA/TMC	6
	PDS	PGA/PLLA	8
10	PDS	PLLA	4
	PDS	PHBA	2
	PDS	PHBA/HVA	1.5
	PDS	Chitine fiber	6
15	PDLLA	PGA	12
	PDLLA	PGA/TMC	8
	PDLLA	PGA/PLLA	10
	PDLLA	PLLA	6
	PDLLA	PHBA	4
20	PDLLA	PHBA/HVA	3
	PDLLA	PDS	1.5
	PLLA	PGA	14
	PLLA	PGA/TMC	6
25	PVA	PGA	20
	PVA	PGA/TMC	14
	PVA	PGA/PLLA	15
	PVA	PLLA	10
30	PVA	PHBA	8
	PVA	PHBA/HVA	6
	PVA	PDS	8
	PVA	Chitine fibers	6
35	<u>PGA/TMC</u>	<u>PGA</u>	<u>4</u>

40 EXAMPLE 4.

Sutures, which were braided of absorbable fibers and monofilament sutures were applied to manufacture by knitting cotton knit type knit fabric. The knit fabric was melted from its one surface by pressing it against a hot steel plate in such a way that the other surface of the knit fabric remained unmelted. The relative tensile and tear strengths of the self-reinforced

absorbable films manufactured in this way were measured by comparing their tensile and tear strengths to the corresponding values of nonoriented, melt-molded corresponding films. The latter films were
 5 manufactured by melting the knit fabrics totally between two hot steel plates. The studied materials are given in Table 4. The relative tensile and tear strengths of self-reinforced films are also given in Table 4.

10

Table 4. Properties of self-reinforced absorbable films

Fiber material	Thickness	R.T.S.	R.Tr.S. of
	of thread (USP)	of film	film
PGA (Dexon)	3-0	6	*
PGA/TMC (Maxon)	1	4	20
PGA/PLLA (Vicryl)	0	5	*
20 PLLA	1	3	12
PDS	1	3	8

*The tear thread broke before the breaking of the
 25 film.

EXAMPLE 5.

PGA-, PGA/PLLA-, PLLA- and PDLA-fibers (thicknesses
 30 10 - 80 μ m) were cut to 20 mm long pieces. The cut fibers were collected on a porous surface by means of suction so that about 200 μ m thick non-woven felts were formed. The felts were compressed mechanically (pressure 80 MPa) into tight films (or membranes)
 35 (thickness about 100 μ m) and they were melted from the one surface by means of a hot plate. The relative tensile strength of the reinforced films were between 1.5 and 3 and the relative tear strengths were between

4 and 7 in comparison to the strength values of totally melted nonoriented corresponding films.

EXAMPLE 6.

5

PGA-, PGA/PLLA- and PLLA-fibers of Example 5 were bound together by mixing into every fiber mass 10 weight-% of finely ground PDLLA-powder (particle size about 1 μm) and by compressing fiber powder mixtures at 150 °C into porous non-woven films, where PDLLA was as a binding material forming a noncontinuous matrix. The relative tensile and tear strengths of these films was between 2 and 8 in comparison to the corresponding values of the totally melted films.

15

Claims:

1. Absorbable and/or soluble polymeric film,
characterized in that it is reinforced at least
5 partially by absorbable and/or by soluble oriented
structural reinforcement elements.
2. A film according to the Claim 1, characterized in
that the oriented structural reinforcement elements
10 are oriented molecular chains or their parts, oriented
crystalline lamellae, spherulites, fibrils or their
parts or corresponding morphological structural
elements.
- 15 3. A film according to Claims 1 or 2, characterized
in that the oriented structural reinforcement elements
are fibers, filaments, film fibers, threads, cords,
non-woven structures, nets, meshes, knits or woven
fabrics or corresponding.
- 20 4. A film according to any Claim of Claims 1-3,
characterized in that it is at least partially porous.
5. A film according to any Claim of Claims 1-4,
25 characterized in that its maximum thickness is 2000
 μm .
6. A film according to any Claim of Claims 1-5,
characterized in that it is manufactured at least
30 partially of at least one of the following absorbable
and/or soluble polymers: polyglycolides (PGA),
polylactides (like PLLA, PDLLA), glycolide/lactide
copolymers (PGA/PLA), glycolide/trimethylene carbonate
copolymers (PGA/TMC), poly- β -hydroxybutyric acid
35 (PHBA), poly- β -hydroxypropionic acid (PHPA), poly- δ -
hydroxyvaleric acid (PHVA), PHBA/PHVA copolymers,
poly-p-dioxanone (PDS), poly-1,4-dioxanone-2,5-diones,
polyesteramides (PEA), poly- ϵ -caprolactone, poly- δ -

valerolactone, polycarbonates, polyesters of oxalic acid, glycolic esters, dihydropyrane polymers, polyetheresters, cyano-acrylates or chitine polymers.

5 7. A film according to any Claim of Claims 1-6, characterized in that it has been reinforced at least partially by means of oriented structural reinforcement elements, which consist of at least one of the polymers: polyglycolides (PGA), polylactides
10 (like PLLA, PDLA), glycolide/lactide copolymers (PGA/PLA), glycolide/trimethylene carbonate copolymers (PGA/TMC), poly- β -hydroxybutyric acid (PHBA), poly- β -hydroxypropionic acid (PHPA), poly- δ -hydroxyvaleric acid (PHVA), PHBA/PHVA copolymers, poly-p-dioxanone
15 (PDS), poly-1,4-dioxanone-2,5-diones, polyesteramides (PEA), poly- ϵ -caprolactone, poly- δ -valerolactone, polycarbonates, polyesters of oxalic acid, glycolic esters, dihydropyrane polymers, polyetheresters, cyano-acrylates or chitine polymers.

20 8. A film according to any Claim of Claims 1-7, characterized in that it includes some biofunctional chemical, like antibiotic, growth hormone, drugs etc. chemotherapeutical chemical.

25 9. A film according to any of Claim of Claims 1-8, characterized in that the film and/or the structural reinforcement elements are oriented bi-axially.

30 10. A method to manufacture the film of any Claim of Claims 1-9, characterized in that at least part of the structural reinforcement elements of material are oriented by means of the flow of the material and/or
35 by means of mechanical deformation or by reinforcing the continuous or noncontinuous matrix by means of absorbable and/or soluble fibers, film fibers or by means of structures which are constructed of them.

11. The use of the film of any Claim of Claims 1-10 in supporting living tissues or organs or their parts or their joining to each other.

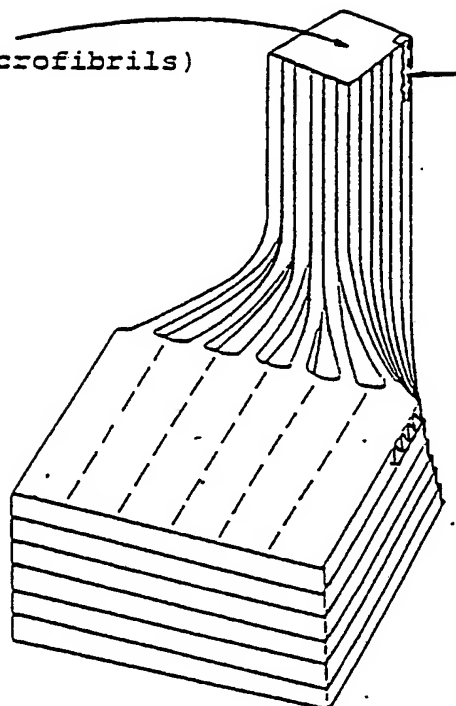
5

12. The use of the film of any Claim of Claims 1-10 to separate living tissues or organs or their parts from each other.

10 13. The use of the film of Claim 12 to protect the controlled growth of the periodontal ligament- and/or cementum tissues.

A fibril (a
bundle of microfibrils)

crystalline blocks

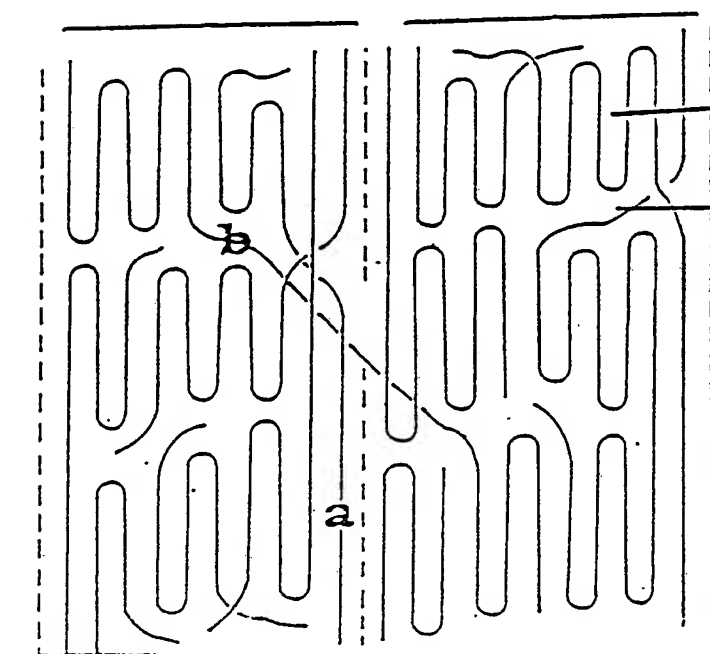


group of lamellae

Figure 1a

Transformation of lamellar structure to fibrillar
structure

microfibrils



a crystalline block

an amorphous region

a = an intrafibrillar
tie-molecule

b = an interfibrillar
tie-molecule

Figure 1b

Microfibrils structure

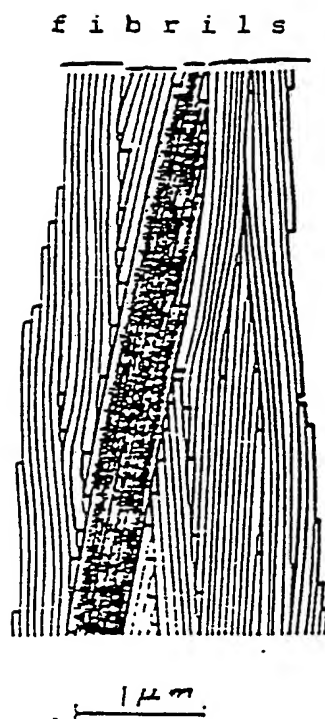


Figure 1c

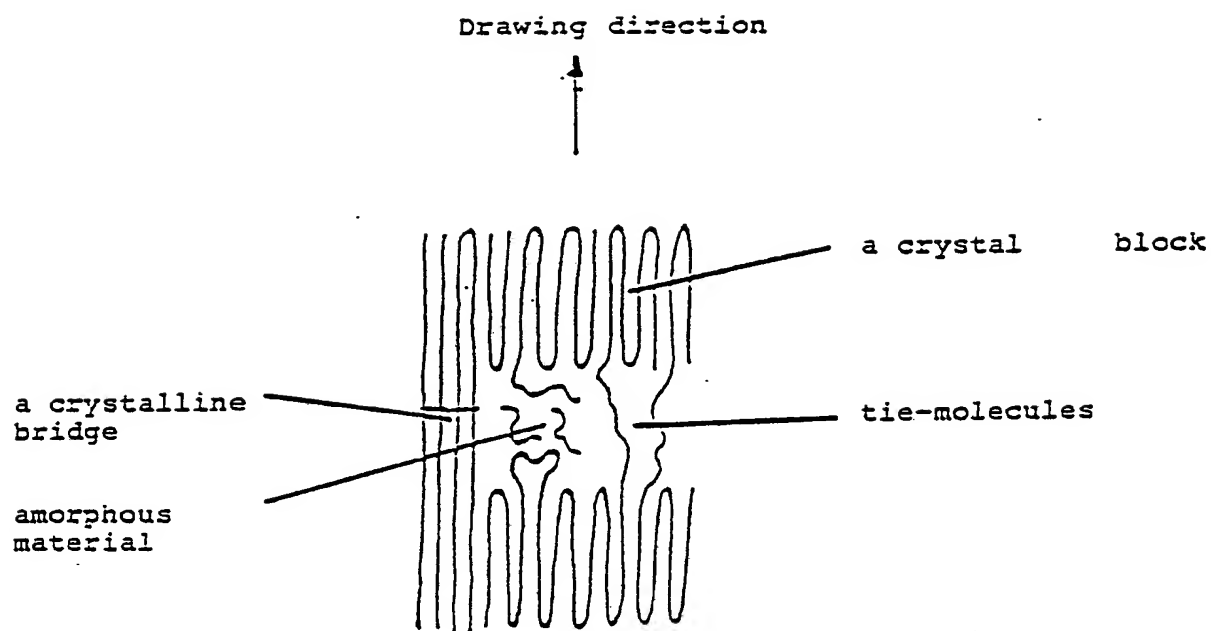


Figure 2

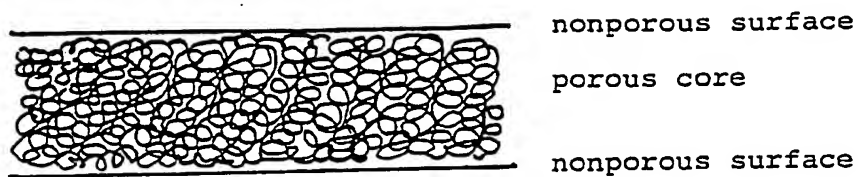


Figure 3.

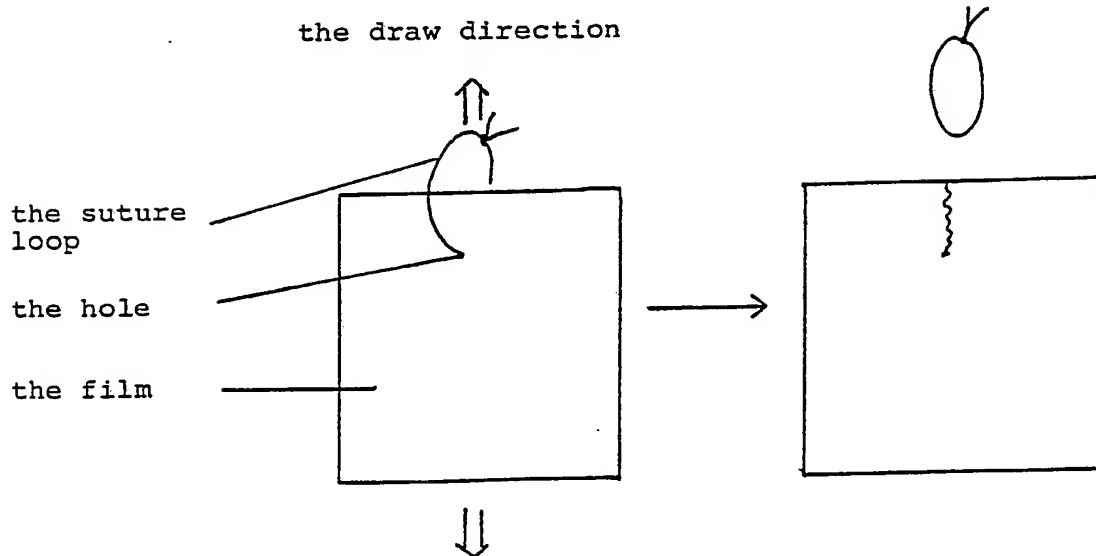
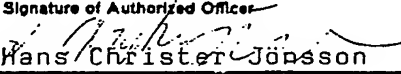
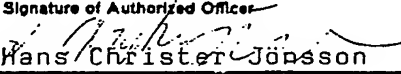
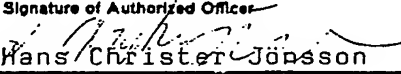


Figure 4.

INTERNATIONAL SEARCH REPORT

International Application No PCT/FI89/00105

I. CLASSIFICATION F SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC ⁴ <div style="text-align: center; margin-top: 10px;">A 61 L 27/00</div>																	
II. FIELDS SEARCHED <div style="text-align: center; margin-top: 10px;">Minimum Documentation Searched ⁷</div> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;">Classification System ⁸</td> <td style="width: 50%; border: none;">Classification Symbols</td> </tr> <tr> <td style="border: none; text-align: center; padding-top: 10px;">IPC 4</td> <td style="border: none; text-align: center; padding-top: 10px;">A 61 L; A 61 F</td> </tr> </table> <div style="text-align: center; margin-top: 10px;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched ⁹</div> <div style="text-align: center; margin-top: 10px;">SE, NO, DK, FI classes as above.</div>			Classification System ⁸	Classification Symbols	IPC 4	A 61 L; A 61 F											
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III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%; padding: 5px;">Category ²</th> <th style="width: 70%; padding: 5px;">Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²</th> <th style="width: 20%; padding: 5px;">Relevant to Claim No. ¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">EP, A2, 0 146 398 (SOUTHERN RESEARCH INSTITUTE) 26 June 1985 see pages 20-21 & JP, 60153868 US, 4655777</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-10</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">US, A, 4 731 074 (EDUARD P.M. ROUSSEAU ET AL) 15 March 1988</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-10</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">EP, A1, 0 204 931 (MATERIALS CONSULTANTS OY) 17 December 1986</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-10</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">Dialog Information Services, File 155, Medline 82105985, Dialog accession no. 04562985, Pilet J et al; "Comparison of poly(dG-dC).poly(dG-dC) conformations in oriented films and in solution", Proc Natl Acad Sci U S A Jan 1982, 79(1) p 26-30 .../...</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-10</td> </tr> </tbody> </table>			Category ²	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	X	EP, A2, 0 146 398 (SOUTHERN RESEARCH INSTITUTE) 26 June 1985 see pages 20-21 & JP, 60153868 US, 4655777	1-10	A	US, A, 4 731 074 (EDUARD P.M. ROUSSEAU ET AL) 15 March 1988	1-10	A	EP, A1, 0 204 931 (MATERIALS CONSULTANTS OY) 17 December 1986	1-10	A	Dialog Information Services, File 155, Medline 82105985, Dialog accession no. 04562985, Pilet J et al; "Comparison of poly(dG-dC).poly(dG-dC) conformations in oriented films and in solution", Proc Natl Acad Sci U S A Jan 1982, 79(1) p 26-30 .../...	1-10
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IV. CERTIFICATION <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; padding: 5px;">Date of the Actual Completion of the International Search</td> <td style="width: 50%; border: none; padding: 5px;">Date of Mailing of this International Search Report</td> </tr> <tr> <td style="border: none; text-align: center; padding: 5px;">1989-09-14</td> <td style="border: none; text-align: center; padding: 5px;">1989 -10- 02</td> </tr> <tr> <td style="border: none; padding: 5px;">International Searching Authority</td> <td style="border: none; padding: 5px;">Signature of Authorized Officer</td> </tr> <tr> <td style="border: none; text-align: center; padding: 5px;">Swedish Patent Office</td> <td style="border: none; text-align: center; padding: 5px;">  Hans Christer Jönsson </td> </tr> </table>			Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	1989-09-14	1989 -10- 02	International Searching Authority	Signature of Authorized Officer	Swedish Patent Office	 Hans Christer Jönsson							
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III. D CUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	Rapra Abstracts, abstract No 7721808L, Shettigar U R: "Collagen film for burn wounds dressings reconstitu- ted from animal intestines", Artificial Organs 6, No 3, Aug 1982, p 256-60	1-10
A	Chemical Abstracts, Vol 108 (1988), abstract No 156432b, Nakamura, T, Adv. Biomater., 7(Biomater.Clin. Appl.), 759-64, 1987	1-10

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☒ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☒ Claim numbers 11-13 because they relate to subject matter not required to be searched by this Authority, namely:

Methods for treatment of the human or animal body
by surgery or therapy, as well as diagnostic methods.

2. ☐ Claim numbers, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim numbers, because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ²

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

- ☐ The additional search fees were accompanied by applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.